

IN THE SPECIFICATION**AMENDMENTS TO THE SPECIFICATION**

1. Please amend the paragraph bridging pages 1-2 as follows:

Mycobacteria is the cause of a number of severe diseases, including tuberculosis, leprosy, and mycobacteria-induced meningitis. Tuberculosis is an ancient scourge of human beings, caused by *Mycobacterium tuberculosis*. Although more than three billion people have been inoculated with the vaccine BCG, presently more than 50,000 people die every week of tuberculosis worldwide, and there are estimates that one third of the world's population is infected by *Mycobacterium tuberculosis*. According to a recent report of the World Health Organization (WHO) on tuberculosis epidemic, distributed via the internet (~~http://www.who.int/inf-fs/en/fact104.html~~), it is estimated that between the years 2000 and 2020, nearly one billion people will carry tuberculosis bacteria, 200 million people will get sick, and 35 million will die of tuberculosis, if control of the disease and preventive measures are not strengthened. Moreover, it has been reported that 32% of HIV infected individuals die of tuberculosis. The situation has become even more dramatic since a number of *Mycobacterium tuberculosis* strains have shown a multidrug resistance, which cannot be attacked by conventional therapy, e.g., antibiotics. In addition, immune-suppressed people similar to AIDS patients are often victims of mycobacterial infections leading to a poor prognosis.

2. Please amend the paragraph on page 4, lines 11-27, as follows:

It has been found that certain disease-inducing factors can be secreted by a cellular organism to the environment of the organism. Specifically, in the present invention it has been found that mycobacterial proteins are secreted from the bacterium *Mycobacterium tuberculosis* to the environment of such a bacterium. One protein which can be secreted by *Mycobacterium tuberculosis* is the serine/threonine ~~protein~~ protein kinase PknG. The fact that the inventive therapeutic compounds described herein are particularly effective against PknG may be due to the fact that this protein kinase can be attacked by these compounds without the need to penetrate the (thick) cell wall of *Mycobacterium tuberculosis*. Consequently, the present invention also discloses the use of at least one serine/threonine protein kinase for developing methods for

detection and/or determination of these kinases for ~~recognising~~ recognizing diseases, for monitoring diseases, and/or for controlling therapy of diseases. Preferably, the methods are immunochemical methods. According to a preferred embodiment of the present invention, the serine/threonine protein kinase used as a target for identifying effective ~~therapeuities~~ therapeutics for inhibiting mycobacterial infections is a mycobacterial protein kinase, particularly the mycobacterial serine/threonine protein kinase G (PknG), which is from *Mycobacterium tuberculosis*.

3. Please amend the paragraph on page 13, lines 1-5, as follows:

Also ~~Preferred~~ preferred are compounds wherein  $R^3$ ,  $R^4$ ,  $R^5$  and  $R^6$  represent independently of each other  $-R^{11}$ ,  $-R^{12}$ ,  $-R^{12'}$ ,  $-OR^{12}$ ,  $-SR^{12}$ ,  $-NO_2$ ,  $-CO-R^{12}$ ,  $-COOR^{12}$ ,  $-CONR^{12}R^{12'}$ ,  $-NR^{12}R^{12'}$ ,  $-SO_2R^{12}$ ,  $-SO_3R^{12}$ ,  $-CH_2OR^{12}$ , and wherein  $R^{11}$ ,  $R^{12}$ , and  $R^{12'}$  have the meanings as defined above in the general formula (I).

4. Please amend the paragraph on page 33, lines 24-30, as follows:

Other aspects of the present invention relate to 4,5,6,7-tetrahydrobenzo[b]thiophene compounds of the general formula (I) as shown above as new pharmaceutically active agents, particularly for the prophylaxis and/or treatment of mycobacteria ~~mycobateria~~-induced infections (including opportunistic infections) and diseases, to pharmaceutical compositions comprising these 4,5,6,7-tetrahydrobenzo[b]thiophene derivatives as active ingredients, and to a method for treating virally and/or bacterially induced diseases, particularly mycobacteria-induced infections, in mammals, including humans.

5. Please amend the paragraph on page 34, lines 13-26, as follows:

The 4,5,6,7-tetrahydrobenzo[b]thiophene compounds as well as pharmaceutically acceptable salts thereof according to the present invention are effective against mycobacteria-induced infections, particularly tuberculosis, but also, e.g., leprosy and mycobacteria-induced meningitis. Mycobacteria which induce or cause these infectious diseases are members of the group comprising the tuberculous bacteria *Mycobacterium tuberculosis*, *M. bovis*, *M. africanum* and *M. leprae* as well as the non-tuberculous bacteria *M. abscessus*, *M. avium*, *M. celatum*, *M. chelonae*,

*M. fortuitum*, *M. genavense*, *M. gordonae*, *M. haemophilum*, *M. intracellulare*, *M. ~~kansii~~ kansasii*, *M. malmoense*, *M. marinum*, *M. scrofulaceum*, *M. simiae*, *M. szulgai*, *M. ulcerans* and *M. xenopi*. Because of the outstanding clinical importance of tuberculosis, microbiologists have distinguished the so-called “Mycobacterium tuberculosis complex” consisting of *Mycobacterium tuberculosis*, *M. bovis*, and *M. africanum* from all other mycobacteria which form the group of the so-called “atypical mycobacteria” or “non-tuberculous mycobacteria (NTM)”.

6. Please amend the paragraph on page 15, lines 15-21, as follows:

Furthermore, the present invention also includes pharmaceutical preparations for parenteral application, including dermal, intradermal, intragastral, intracutaneous ~~intraeutan~~, intravasal, intravenous, intramuscular, intraperitoneal, intranasal, intravaginal, intrabuccal, percutaneous, rectal, subcutaneous, sublingual, topical, or transdermal application, which preparations in addition to typical vehicles and/or diluents contain at least one 4,5,6,7-tetrahydrobenzo[b]thiophene compound and/or a pharmaceutical acceptable salt thereof as active ingredient.

7. Please amend the paragraph bridging pages 35-36 as follows:

The pharmaceutical compositions according to the present invention containing at least one 4,5,6,7-tetrahydrobenzo[b]thiophene compound as described herein and/or a pharmaceutical acceptable salt thereof as active ingredient will typically be administered together with suitable carrier materials selected with respect to the intended form of administration, i.e. for oral administration in the form of tablets, capsules (either solid filled, semi-solid filled or liquid filled), powders for constitution, gels, elixirs, dispersible ~~dispersable~~ granules, syrups, suspensions, and the like, and consistent with conventional pharmaceutical practices. For example, for oral administration in the form of tablets or capsules, the active drug component may be combined with any oral non-toxic pharmaceutically acceptable carrier, preferably with an inert carrier like lactose, starch, sucrose, cellulose, magnesium stearate, dicalcium phosphate, calcium sulfate, talc, mannitol, ethyl alcohol (liquid filled capsules) and the like. Moreover, suitable binders, lubricants, disintegrating agents and coloring agents may also be incorporated into the tablet or capsule. Powders and tablets may contain about 5 to about 95 weight % of the

4,5,6,7-tetrahydrobenzo[b]thiophene compound or the respective pharmaceutically active salt as active ingredient.

8. Please amend the paragraph on page 45, lines 10-11, as follows:

Oral gels refer to the active ingredients dispersed or ~~solubilised~~ solubilized in a hydrophilic semi-solid matrix.